REMARKS

Status of Claims

Claims 1-56 are subject to a restriction requirement. Claims 1, 4-12, and 15-56 are provisionally withdrawn, with the intention of rejoinder if the restriction requirement is withdrawn. Claims 57-59 are cancelled.

Restriction Requirement

In the Office Action of August 20, 2008 the Examiner poses a 6-way restriction requirement, requiring Applicant to select from

Group 1, claims 1, 3-12, and 15-29, drawn to RNA expression based methods for detection of SIRS;

Group 2, claims 1 and 13, drawn to RNA expression based methods for detection of sepsis and/or sepsis like conditions;

Group 3, claims 3 and 14, drawn to RNA expression based methods for detection of severe sepsis;

Group 4, claims 30, 33-39, and 42-56, drawn to peptide based methods for detection of SIRS;

Group 5, claims 31 and 40 drawn to peptide based methods for detection of sepsis and/or sepsis like syndrome; and

Group 6, claims 32 and 41 drawn to peptide based methods for detection of severe sepsis.

In response, Applicant elects Group 2, with traverse, for the reason that at least Group 3, if not all groups, should be grouped with Group 2.

Applicants note paragraph 3 of the Restriction Requirement wherein the Examiner characterizes the "common technical feature" as use of genes associated with various sepsis related conditions. This is not entirely correct - it is not use of genes, but measurement of LEVELS of genes, that is the common technical feature.

Applicants explain that the claims all fall under one single unifying concept: The invention is based on measuring the level of RNA/product. All current claims are directed to a quantitative detection of expression levels, and not to the mere (rather qualitative) determination of the presence of a certain gene or product.

The "common inventive feature" of the present invention is that the present invention is based on the discovery that diagnosis can be made using body fluids and detecting

- RNA levels different from normal levels, or
- RNA derived peptide levels or
- peptide segment levels derivable from RNA levels.

This is a departure from the closest prior art, which uses microarrays or clinical appearance as diagnostic tool. According to the specification:

> To differentiate between symptoms that base on microbial infections and other symptoms of non-infectious etiology, which could indicate sepsis due to their **clinical** appearance, but are in fact not based on a systemic microbial infection, e.g. of symptoms that base on non-infectious inflammation of individual organs, the determination of gene expression profiles via differential diagnostics proved to be particularly advantageous [19-22]. The use of body fluids for the measurement of gene expression profiles for the diagnosis of SIRS has not yet been described.
>
> The point of origin of the invention disclosed in the present patent application is the realization that **RNA levels** different from normal values respectively **peptide levels or peptide segment levels** derivable from the RNA levels, that can be detected in a serum or plasma of a patient whose risk is high that he will be suffering from SIRS, or who suffers from symptoms that are

typical for SIRS, can be detected before SIRS, sepsis, sepsis-like conditions, severe sepsis and systemic Infections are detected in biological samples.

The invention is not in detecting presence of particular genetic material (as could be done with a micro-array / chip), but rather, in detecting level of activity (as could not be done with a chip). Our claims require "quantitative" detection, comparing, and determining whether the genetic activity is more or less than standard.

Applicants measure the activity not of only one gene, but 2-100, or at least 200, or 200 to 500, or 500 to 100, or 1000 to 2000 genes. The prior art does not teach this type of data extraction and analysis, which characterizes the present invention.

Thus, it is respectfully submitted that all claims recite a common unifying feature and should be considered together.

As a minimum, at least the invention according to claims 2, 3, 13 and 14 should be examined together. Examination in a single application would not be unduely burdensome on the Examiner as these claims can easily be searched and examined at the same time. The Examiner has provided no showing that it would be burdensome to examine these claims togher.

Finally, Applicants submit, pursuant to MPEP section 803, that that the invention of claims 2, 3, 13 and 14 would have been obvious over each other. If there is an express admission that the claimed inventions *>would have been< obvious over each other within the meaning of **35 U.S.C. 103**, restriction should not be required. *In re Lee,* 199 USPQ 108 (Comm'r Pat. 1978).

Further Lack of Unity Requirement

In view of election of Group 2, the Examiner requires Applicants to select a single specific combination of genes. In response, Applicants select the following list (72 Seq-IDs) which are disclosed in the present application, with traverse:

Seq ID	Patent Seq ID	Accession No
220	I.220	(AI540783)
303	I.303	(AI149693)
529	I.529	(AA280062)
754	I.754	(AA150160)
844	I.844	(AA035016)
1705	I.1705	(R70541)
2370	I.2370	(AI888493)
2449	I.2449	(AI821631)
2468	I.2468	(AI820576)
2481	I.2481	(AI811413)
2709	I.2709	(AI732517)
2831	I.2831	(AI675585)
2928	I.2928	(AI623567)
2948	I.2948	(AI613016)
3068	I.3068	(AI554111)
3079	I.3079	(AI539445)
3209	I.3209	(AI364529)
3268	I.3268	(AI343613)
3305	I.3305	(AI273261)
3317	I.3317	(AI281098)
3331	I.3331	(AI224886)
3399	I.3399	(AA868082)
3424	I.3424	(AA833528)
3433	I.3433	(AA812763)
3482	I.3482	(AI214494)
3508	I.3508	(AI221860)
3523	I.3523	(AI218498)
3624	I.3624	(AI217376)
3676	I.3676	(AI148246)
3765	I.3765	(AI041544)
3796	I.3796	(AI003843)
3873	I.3873	(AA947111)
3879	I.3879	(AA923246)
3881	I.3881	(AA923169)
3917	I.3917	(AA825968)
4060	I.4060	(AA708806)
4096	I.4096	(AA682790)
4122	I.4122	(AA478996)
4141	I.4141	(AA417348)
4268	I.4268	(AA417792)
4328	I.4328	(AA493225)
4450	I.4450	(AA495787)
4528	I.4528	(AA453996)
4609	I.4609	(AA412166)
4654	I.4654	(AA398757)
4695	I.4695	(AA035428)
4705	I.4705	(AA029887)
4937	I.4937	(W04695)
5265	I.5265	(H91663)

5338	I.5338	(H65331)
5418	I.5418	(R94894)
5542	I.5542	(H18649)
5567	I.5567	(H16790)
5647	I.5647	(H06263)
5779	I.5779	(R43301)
6018	I.6018	(R12411)
6200	I.6200	(T78484)
6250	II.8	(BC018761)
6251	II.9	(XM_030906)
6259	II.17	(NM_001562)
6267	II.25	(NM_001560)
6271	II.29	(XM_036107)
6297	II.55	(XM_041847)
6314	II.72	(NM_001511)
6327	II.85	(XM_007258)
6334	II.92	(XM_010807)
6341	II.99	(NM_022162)
6342	II.100	(NM_001199)
6346	II.104	(NM_003188)
6359	II.117	(XM_039086)
6365	II.123	(NM_000565)
6366	II.124	(NM_002211)

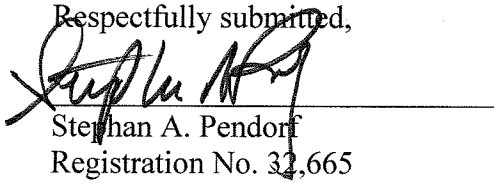
Traversal is for the reason that in accordance with the present invention sepsis conditions are determined not by qualitative measurement of any particular genes, but by quantitative measurement. Thus, to require restriction of the inventnion to any particular combination of genes indicates that the invention is not understood.

Further, Applicants do not understand the relationship between the "Restriction" (different inventions), "Election" (different species but same invention) and "further Lack of Unity" (under which the Examiner requires Applicants to elect species of gene for claims reciting genes, but apparently continues to indicate that the broader claims, which do not recite specific genes, will be examined without being limited to specific claims.

Thus, finally, Groups 2 and 3, with regard to the sepsis related conditions, if the Examiner correctly understands the present invention, then these Groups **should be considered as one invention together with the enclosed sequences**.

The Commissioner is hereby authorized to charge any fees which may be required at any time during the prosecution of this application without specific authorization, or credit any overpayment, to Deposit Account Number 16-0877.

Respectfully submitted,



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Date: **November 20, 2008**